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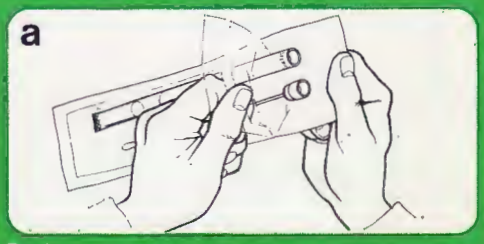

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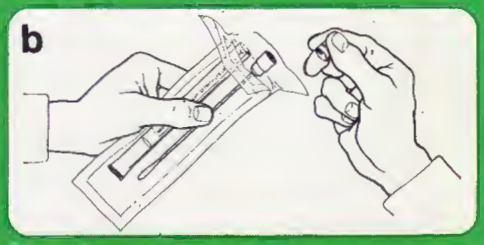

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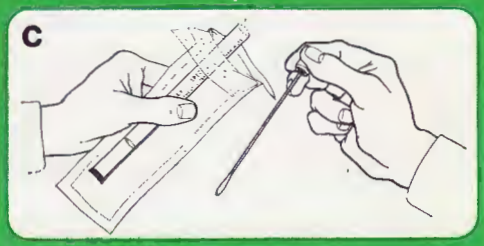

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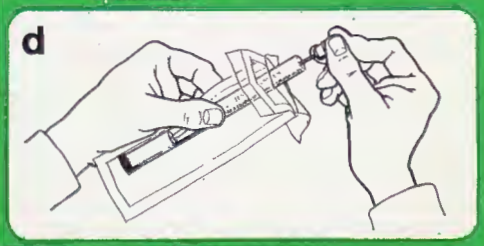

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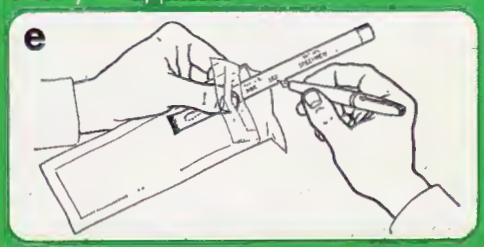

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The Rising Laboratory Workload
A Critical Appraisal of Cause and Effect

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Introduction

There has been a marked increase in spending on public hospitals over the past several years (Figure 1). The increase corrected for the Consumer Price Index on the base year 1970/71 shows nearly 100 percent increase over the period 1970/71 to 1974/75. Increases of this magnitude present service problems which confront most aspects of the entire health service in developed countries where health now ranks among the three largest service industries. In the hospital laboratory services there has been an even greater increase in spending. During the same period and applying the same corrections there has been approximately a 130 percent increase.

It is acknowledged that modern medicine demands a certain level of supportive technology particularly in the diagnostic area, but questions relating to the cost effectiveness of rising levels of expenditure remain unanswered. In the medical laboratory area the rising workloads and consequent rising costs are often viewed with complacency. It is generally accepted that all the work is necessary, the results are serving a useful purpose, and the laboratory is simply responding to clinical demands. What the real clinical demands are, once again, remains an unanswered question.

In Pathology Departments we have sheltered under this umbrella of confusion in not separating demands from needs and have in fact added to this confusion by the introduction of practices, some of which may not be entirely justified. For too long we have accepted that all demands should be met and have not examined closely enough the impact of introducing, for example, such practices as admission profiling, block testing, and the type of request form we put into use. We do not always recognise that a proportion of the information we release is not required, is incorrect, is confusing and often useless. We do not question the implications on a regional level, let alone on a national basis,

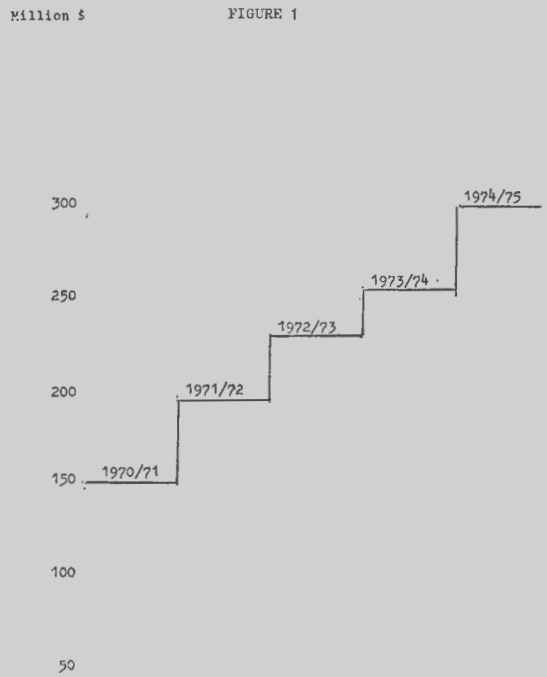

Figure 1. Increases in hospital spending after correction for inflation.

of our developments, some of which may be a form of local empire building. We do not run audits on the consumers of our service and we pay only lip service to the education of the modern medical student in terms of the proper role of the laboratory in medicine. We succumb to the pressures of the purveyors of medical aids for the performance of more and more tests and we generally fail to practise good management in the provision of our service. Those who wish to increase or improve services in these supportive areas are usually not as restrained when it comes to spending public money as they would be in their own spending.

This study is an attempt to examine some of the problems relating to the use and abuse of laboratory services.

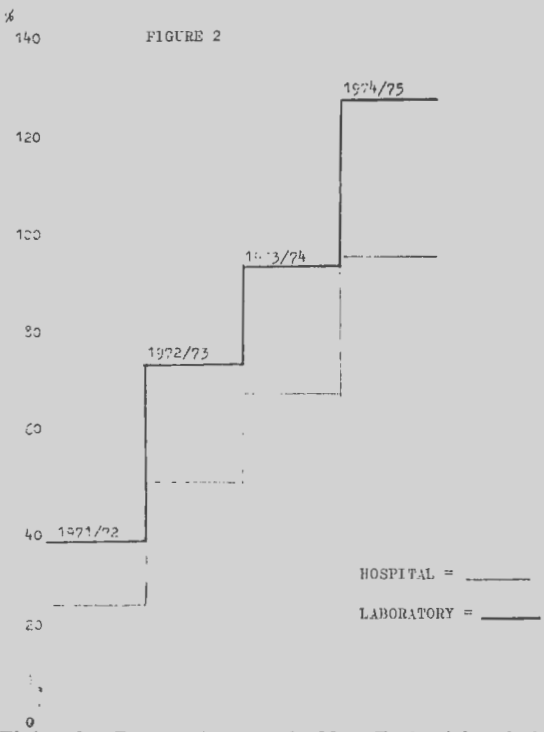

Figure 2. Percent increase in New Zealand hospital spending compared with laboratory services after correction for inflation.

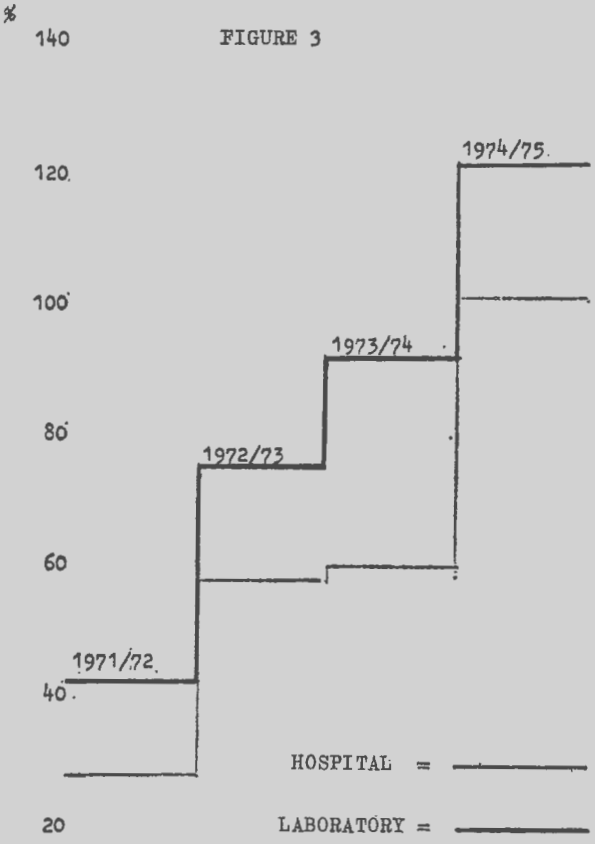

Figure 3. Percent increase in laboratories compared with hospital spending for Auckland Hospital Board's institutions corrected for inflation.

The Rising Expenditure on Laboratory Services

Although there is an abundance of information available on laboratory "test" numbers, laboratory costs and staffing, hospital admission figures, etc., the interpretation of this information becomes difficult when, for example, the following factors are taken into account:

1. Inflation.
2. Acquisition by laboratories of multi-channel analytical equipment.
3. Changes by the laboratory in requesting forms which allow for "block" testing.
4. Doubtful accuracy of laboratory statistic collection.

Because of the difficulty in defining a "test" and the consequent suspected accuracy of statistic collection, it becomes even more difficult to determine the extent of increasing laboratory workloads.

One way of looking at this problem is to compare the spending by laboratories as a percentage of the health vote using the year 1970/71 as a base (Figure 2). This shows that when hospital and laboratory costs are corrected for the Consumer Price Index, hospital costs have risen by nearly 100 percent and laboratory costs by nearly 130 percent. The same supporting evidence can be obtained by examining similar figures for the Auckland Hospital Board's four main institutions, Auckland, Green Lane, Middlemore and National Women's Hospitals (Figure 3). When corrected for inflation the hospital has a 100 percent increase, with the laboratory 122 percent. It is concluded from these figures that the hospital laboratory services are growing

at a faster rate than the remainder of the hospital service.

Reasons Advanced for the Rising Workload

1. *Profiling in Clinical Biochemistry and Haematology*

The development by Skeggs in 1957 of the continuous flow principle and the subsequent production of autoanalysers have had a profound effect on the operation of medical laboratories. Even more so, the grouping of such analysers into multi-channel instruments has permitted laboratories to carry out biochemical profiles.

The acquisition of these instruments has resulted in the development of a new breed of laboratory worker, one who has an interest in the production line, or factory-type operations of a large biochemistry department. This has prompted Astrup[1] to state "the departments more and more seem to resemble 'supermarkets' where the customers just get their articles and where interchange between customers and dealers is reduced to complaints when articles are not available in sufficient amounts or of a satisfactory quality." The result of this technological development has been the easy production of more test results and because of the inflexibility of some of these instruments this has meant that the doctor, regardless of his actual requirements, usually gets many more results than requested. This in turn has created a cycle with the laboratory because of data-handling problems from multi-channel instruments requiring more money for computerisation and the cycle is continued by the analyser manufacturer producing even larger instruments.

Annual growth rates for laboratories are stated to be of the order of 10-20 percent per annum and this is well documented but there is a dearth of information as to the proportion of these increases which have resulted from the use of multichannel instruments for analysis.

Early enthusiasts for biochemical profiling of about 9-10 years ago used the arguments that profiling was cost justifiable, was useful for detecting pre-symptomatic conditions and was in fact a requirement of medical staff. More recently the literature indicates an increasing disenchantment with this concept. Whitehead and Wootton[20] carried out biochemical admission profiles in two British hospitals. They totalled 31,439 tests and found that only 23 percent of these tests were being requested. Of the unrequested tests 71 percent were normal, 3.5 percent were abnormal, unexplained, and only 0.7 percent were abnormal but provided diagnostic information. Further, they found no large numbers of new unexpected diagnoses, no dramatic changes in treatment and no alteration in day-stay.

Durbridge[5] and others in an Australian study compared the progress of test patients who had an automatic admission profile, against a control group. They concluded, despite the rapid delivery of results, that the profile had no effect on mortality or hospital stay, duration of all monitored clinical signs was unaltered, medical opinion on the progress of profiled patients was not altered, there was no improvement in bedside nursing activity, nor was there any advantage from profiling in doctor attendances for the patients, clinical consultations, surgical procedures, prescriptions, para-medical services or bedside equipment usage, or improvement in the speed with which treatment was begun. Further, they found only one-third of the tests performed were actually requested and more tests were requested on the second round of testing on profiled patients than on the controls. This resulted in 78 percent more investigations on profiled patients with a consequential 64 percent increase in the costs of investigations and a 5 percent increase in the costs to the hospital. Their final conclusion was that admission multiphasic profiling was not cost justified and they did not advocate its introduction.

Bradwell[3] and others examined 200 patients who had unexplained unexpected abnormal results from a biochemistry profile performed five years previously during an admission to hospital. Only three patients had results which indicated a pre-symptomatic disease, although the possible effects of earlier treatment of these three patients in 1967 when they were first admitted to hospital was unknown.

Leonard[13] and others carried out biochemistry profiles on 2,816 children in two controls trials and concluded that day-stay was not altered but that there was a significant increase in requests resulting from the profile. They con-

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cluded that the results from the profile made "only a small contribution to overall care of patients."

Holland[9] in his summation of a Lancet series "Screening for Disease," states, "with multiple tests undertaken on admission to hospital, it is more difficult to define normality and the results of studies in this area are so far inconclusive. Supporters of such tests contend that they are simpler and cheaper but whether this is so, is far from clear. The alternative view that they lead to further investigations, longer stays in hospital and increased uncertainty for the patient, has not yet been convincingly disproved. Of the many biochemical abnormalities picked up by profiles, either on admission to hospital, or in the context of a well person screening programme as described by Bailey[2], few seem to be indicative of disease at a pre-symptomatic stage. Thus, whatever their economic and administrative advantages, biochemical profiles make poor screening tests".

In fact, a number of the workers cited above have already demonstrated that there is an increase in second-line requesting once the biochemical profile has been done. Schoen[16] has also observed that unsolicited abnormal chemistry findings lead to a great deal of additional studies. Unfortunately, 80 percent of these additional studies led to conclusions having no clinical significance for the patient. He also noted that 70 percent of the significant abnormal unsolicited chemistry findings were related to blood glucose and urea estimations which is similar to Sims'[18] findings. Sims also found in his 1969 survey carried out at Green Lane Hospital that there was a very large increase in tests ordered after profiling.

It is suggested from the more recent literature on biochemical profiling in hospitals that there is a lack of evidence to support from a clinical point of view any real benefits to patients or to hospital administration in terms of improved patient turnaround. It is also suggested that profiling significantly increases the number of laboratory tests requested.

2. *Effects of Providing Blood Collecting Services*

Over the years there has been a growing trend towards providing blood collection under the control of the laboratory services. This has resulted in either the extensive use of laboratory technical staff or the employment of specialised staff, often registered nurses, for blood collection. The arguments usually given to support this practice are

(i) patients usually receive better service from highly specialised staff.
(ii) The laboratory, through control of collection of its specimens, is better able to schedule its work.
(iii) There is considerable time-saving for house surgeons when they do not have to collect their own blood samples.

However, the other side of the story often presents as abuse of this service and results in increased laboratory testing. When one considers for example, just how easy it is for the house surgeon to ask for large numbers of tests by simply ticking the appropriate box on the request forms and leaving them in the ward for processing by collection staff, it can readily be seen how the system can be abused.

What is more, this system can also result in a lack of awareness by the house surgeon and nursing staff of the discomfort to the patient because of their relative non-involvement. For instance, there may be difficulty in locating a patient's vein, the amount of blood to be drawn may be very large because of the number of tests requested, or fasting patients may be taken to another department before blood glucoses have been collected.

TABLE I

Ordinary Monday	182
Public Holiday Monday	86
Ordinary Friday	205
Public Holiday Friday	82

Comparison of bloods collected for Clinical Chemistry by blood collectors on ordinary days and house surgeons on Public Holidays.

To demonstrate that at least some measure of over-requesting is brought about by providing a blood collection service, two public holidays were compared with the same ordinary working days for numbers of in-patient bloods collected for clinical chemistry tests by house surgeons on public holidays and laboratory collectors on ordinary working days. The results in Table I indicates a decrease in requests of approximately 60% when house surgeons collect their own

samples. This was despite the fact that admissions to the hospital and medical and nursing staff were at normal week-day operating level. There also appeared to be no significant increase in requesting on the day following the public holiday.

3. Laboratory Request Forms

The layout of the laboratory request form has a marked influence on the way in which tests are ordered. One of the best examples of this can be seen by the way the laboratory influences requesting to suit particular types of analytical equipment. For instance, at Auckland Hospital, the laboratory has both 12 and 6 channel machines which provide respectively tests called Block B and Block A. Doctors for a number of years by ticking one or the other block on a request form will have reported back to them either 12 tests or 6 tests. This, despite the fact that they may only wish to have one or two tests from the block. Obviously this practice will increase considerably the test numbers and have a falsifying effect in that many of the tests recorded may not have actually been asked for at all.

To test the effect of block testing an experimental request form was designed simply listing all tests individually. The form was placed in two surgical and two medical wards for four weeks. During this time 150 individual requests were received, the requests were directed to either the 6 or 12 channel machine but of the total tests performed only 62% were actually asked for on the experimental request form.

4. Decreasing Day Stay

Decreasing the day stay of patients will cause an increase in workload. This is shown in Fig. 4. There is a heavy requesting load on admission and a gradual diminution until discharge. Hospitals with a shorter day stay will obviously be required to process more tests which in turn will increase costs. This is obviously not appreciated by those who consider that improvements in service which may reduce day stay is cost justified. The argument that is often put forward states that steps taken to reduce a patient's stay in hospital will reduce costs. In fact the opposite is true for no sooner is the patient discharged than the vacated bed is filled by a new high cost patient. The problem is further compounded by increasing

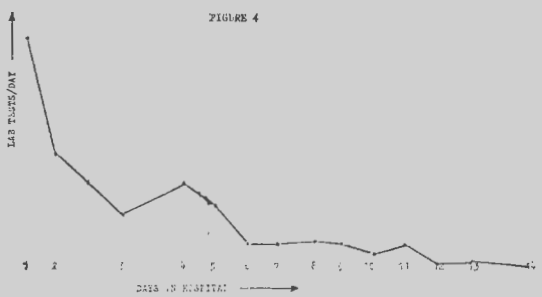

Figure 4. Increasing workload related to decreasing day stay of patient.

requests for numbers of tests per patient. For instance, at Auckland Hospital, there has been a 21% increase in tests per patient during the period 1970 to 1975.

5. The Ward Routine

In theory, doctors should be requesting tests with a full knowledge of the "sensitivity and specificity of the test with the incidence of the disease in the population tested" as indicated by Krieg et al[11] and also with at least some knowledge of the cost effectiveness of the tests requested.

They should be able to interpret the results with an understanding of the limitations of derived reference ranges, of the experimental error as indicated by the precision limits of the tests and of other factors such as drug interference, etc.

Unsuspected abnormal results should not be dismissed nor should they be automatically repeated without consultation. In summary Krieg and La Combes'[12] statement is worth repeating. They suggest that before ordering tests doctors should:

(i) attempt to determine whether test sensitivity, specificity and predictive value are adequate to provide clinically useful information.

(ii) Ask themselves will the results of the tests change the diagnosis, prognosis or therapy.

(iii) Ask themselves will results of this test provide a better understanding of the disease process in this patient.

(iv) Ask themselves what they are looking for and why and will the patient benefit if they find it.

These statements were prefaced by the words "in theory." Even with only a superficial

examination it is evident that the practicalities of ordering laboratory tests are far divorced from the theory.

It is not suggested that all of the tests that are ordered are not used for the patient's benefit, but it is suggested that because of a number of other factors over-ordering often takes place.

One of these factors is based on the ward routine where ordering takes place on the basis of standard procedures rather than on any discriminative basis.

It is sometimes suspected that the routine performance of large numbers of laboratory tests particularly on a continuing basis once patients have been admitted, has a low yield of new, useful information. It is agreed that some testing is necessary for monitoring therapy but even the amount of this type of work processed is suspect. Dixon et al[4] claims that chemistry tests actually used in diagnosis is as low as 5%. Furthermore they reduced the work load by 25% without eliminating any essential information. To test the usefulness of this continued testing Griner and Liptzin[8] withheld the white cell differential count on 37 patients without the results apparently being missed. In Auckland Hospital 142 individual patients' biochemistry and haematology reports were withheld from two surgical and two medical wards for 24 hours after completion. The ward sisters were telephoned to inform them that results were immediately available if required. Only two calls for results were made.

Another example of ward routine affecting laboratory workloads and the indiscriminate use of laboratory services can be seen in the way in which laboratory request forms are made out several days in advance for routine tests. This is done regardless of the latest results or the condition of the patient.

Such routine requesting often leads to lack of documentation in the patient's case notes on tests requested. Two hundred patients' records from surgical and medical wards were examined to determine whether or not laboratory requests were documented as part of the patient treatment. It is agreed that the amount of documentation will vary from house surgeon to house surgeon depending upon their workload, but in this examination of patient records only 43% of requests were recorded in the case notes. This has further implications from the laboratory point-of-view for often telephone calls are received for results of tests never sent to the laboratory and on which there is no documentation in the patient's case notes.

6. Unsuspected Diagnoses

It has been suggested that batteries of laboratory tests requested on a routine basis are necessary to pick unsuspected diagnoses. Small gains from this approach have already been discussed in section 1. There are also inherent problems in this approach due to the lack of an adequate definition of normalcy. Sunderman[19] and Murphy[14] have shown that on the basis of one laboratory test 95% of individuals will be normal and in a battery of 20 tests only 36% of patients will have all values that are normal.

Failure to respond when abnormalities are reported is another problem which may in part be due to the large amount of data produced by the laboratory in response to requests for batteries of tests. Williamson[22] went to some lengths to point out abnormalities on report forms even to the extent of covering abnormals with fluorescent sticky tape. Schneiderman[15], Edwards[6] and Schroeder[17], have all reported similar problems. A good example of this is the routine testing of all patients admitted to the psychiatric ward at Auckland Hospital and to Carrington Psychiatric Hospital. The routine for these patients is a Wasserman, a 12-test biochemistry profile and a 6-test haematology profile. The analysis of 100 patients' biochemistry and haematology results and 550 Wasserman resuts were documented. Suffice to say that the relatively small returns from traditional testing patterns notified to the medical staff at these hopsitals resulted in a 50% decrease in their routine testing.

7. Influence of the Recent Literature

Most laboratory administrators are aware of the pattern that follows the publication of new methods. The pattern that develops results in first of all a small number of requests followed by a gradual build up. The equipment manufacturers eagerly seize on this development, machines are produced and the larger laboratories seek capital funds for their purchase. A vicious cycle is now created because the laboratory which may previously have operated some sort of vetting system on request

forms, now finds with its increased capacity to test that it may be easier to simply process all requests. On occasions these tests may even be brought into the routine for all samples regardless of a specific request.

Both parties are guilty, the requesting doctor and the laboratory for creating a situation which is gradually getting out of control. To demonstrate this effect, a test, the estimation of immunoglobulins, was selected. The immunoglobulins are a group of proteins having overall similarity and also having the ability to act as antibodies. Blood levels are altered in a great variety of conditions.

Immunoglobulin quantitation became available about 10 years ago and was routinely available in this laboratory from about 1970. Figure 5 shows the increase in requests for this test over the period 1971 to 1976. This relatively expensive test shows in fact approximately a 60% increase over the period. One might assume because of the very few requests that are made to the laboratory for assistance in interpretation that there is a fairly high level of understanding of this test. To determine the level of understanding of immunoglobulin quantitation, it was decided, in conjunction with the Specialist Medical Tutor, to run a short test on medical registrars. A multi-choice paper of 10 questions was prepared and marked by the head of the Immunology Department, Associate Professor J. D. Wilson. The test was adjudged by him to be basic.

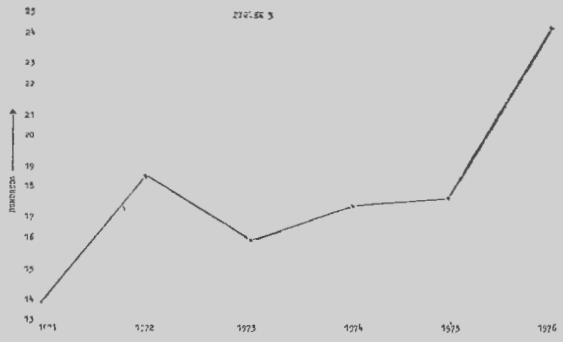

Figure 5. Immunoglobin increase 1971-76.

The result of the test sat by 13 medical registrars gave a mean percentage of 33 with a spread of results between 0 and 50%. The conclusion that can be drawn is that even at relatively senior medical level there is a poor understanding of the interpretation of a relatively new laboratory test. What it the level likely to he with more junior staff?

8. Effects of the Medical School

It has been an "impression" that wards with a direct Medical School involvement request more laboratory tests than other wards. Griner[8] in an American study in a teaching hospital, states that excessive use of the laboratory got to the point where laboratory tests made up 25% of the total hospital bill per patient. The hierarchial system within some of these wards may tend to exert pressure downwards causing house surgeons to over-order tests so that they may be adequately "covered" at ward rounds. Griner[8] in the same study, has stated that the over-use of the laboratory may be due to the "working up" of a patient in order to satisfy one's peers.

TABLE II

A comparison of laboratory tests carried out in general medical and surgical wards with Departments of Medicine and Surgery.

Medicine	**Tests per Patient**
General	13
Department of Medicine	27
Surgery	
General	6
Department of Surgery	9

To demonstrate this effect a medical and surgical ward with direct Medical School involvement was compared with two wards without such involvement. Table II shows that the wards with the Medical School involvement ordered 50% more tests in surgery and 100% more tests in medicine than in general wards.

TABLE III

A comparison of laboratory tests carried out on pneumonia cases admitted to general medical wards and Department of Medicine.

General	9 tests per patient
Department of Medicine	15 tests per patient

A comparison of laboratory tests carried out on thyroid cases admitted to general surgical wards and the Department of Surgery.

General	5 tests per patient
Department of Surgery	9 tests per patient

It could be argued that some of the more unusual cases were admitted to these wards

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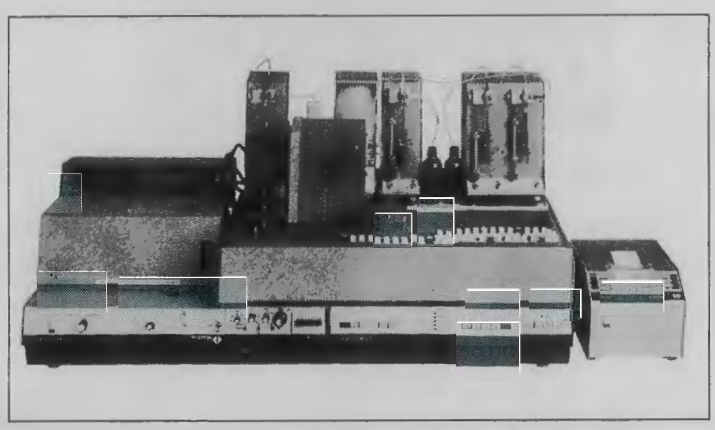

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which would probably account for a greater number of laboratory tests. However, when routine cases are examined in both areas, as seen in Table III, there is still a significantly higher proportion of laboratory tests per case in Medical School-involved wards.

Impact of Laboratory Services on Hospital Admissions

Hospitals exist to treat sick people. The output of hospitals is accordingly treated patients. The resources needed to manage the output is essentially money. This simple systems analysis approach become complicated because although the inputs can be measured in terms of dollars, there is no satisfactory complete measure of the effectiveness of patient treatment. The problem is even further compounded when one considers the statement from WHO[21], " One fact clearly emerges; there is no predictable relationship between improved health on the one hand and the amount of cost of resources used in producing health services on the other. For instance, the indicators of one Latin American country show no improvement in health over the decade in spite of high and increasing ratio of physicians and of hospital beds to population. There has been no successful and agreed index of population health statistics in any country." Although this reference uses the term " health " one could equally apply this statement to hospital treatments. Further it is generally agreed that whatever the resources made available in the health area there would still be insufficient to meet demands.

In the pathology area there is just as surely no satisfactory measure of impact on patient treatment. Statements are made about the laboratory role in improved diagnosis and management, but to back these statements up with a performance measurement is not possible. Griner et al[8] reported on a study of two groups of patients with a diagnosis of diabetes ketoacidosis but despite an increase of about 25% in laboratory tests per patient, there was no apparent improvement in management nor in day stay. Similarly over the period 1962-72 despite expanding technology, the national death rate figures in New Zealand for eight major disease (see Table IV) shows totally no real improvement.

TABLE IV

DEATHS - [illegible]

Source - "Trends - Health and Health Services 1975"

Condition	Deaths		Rates/100,000 population	
	1962	1972	1962	1972
[illegible] DISEASE - all forms except congenital	7607	8494	* 3.6	385
CANCER, MALIGNANT DISEASE	4597	4526	145	155
CARDIOVASCULAR DISEASE	3729	3447	110	118
[illegible] AND LEUKAEMIA	1441	1072	52	37
[illegible] LYMPHOMA AND MYELOMA	772	1030	31	35
DISEASES OF THE ARTERIES *	435	701	18	24
DIABETES MELLITUS	277	459	11	16
DISEASES OF THE KIDNEY AND [illegible]	292	280	12	10
			86	85 average

* Except cerebral, cardiac and hypertensive renal disease.

Discussion

1. The Spending Spree

The so-called " health vote " for 1974-1975 nearly $500 million, which represents nearly 20% of the entire budget for the country. A better term might be " the ill-health vote " because nearly 70% of this vote was spent on hospitals. When one adds to this the increasing figure paid into private medical insurance schemes one cannot help but conclude that we are indeed a sick nation. For the same year nearly $20 million was spent on both private and hospital laboratory services. Was value obtained from money spent? There are probably no real criteria that can be employed to answer this question. Current thinking requires a " cost benefit analysis " or " cost effectiveness analysis " which has little meaning in a hospital laboratory because very often both the demand and supply is generated within that organisation. As far as a cost effectiveness analysis is concerned there seems no adequate measure of the laboratory's role in patient management and care.

One thing is certain and that is the laboratory services are open to serious abuse both by the generators and consumers of the service. Some overseas practices involving massive increase in payments following the introduction of " socialised medicine " have highlighted this

fact. To return to the national scene, it is obvious that the allocation of central government funds is a political decision, and this being the case "health funds" can only be increased at the expense of some other allocation. What is happening increasingly is that hospital boards which are running short of funds seek more from central government. They are told to live within their allocation and if necessary reappraise priorities. The ball is in turn then placed back in the court of the local hospital adminstrators who in general are not in good shape to resist or appraise the often emotional and political arguments of medical staff.

Somewhere along the line, sound management has to prevail or local decision making will be further eroded by an increasing bureaucracy.

2. The Waste

This project started out to collect data on the pathology requesting patterns. It has developed to include an assessment of that data in the light of expanding laboratory services. The broad conclusion reached is that considerable waste exists in the ordering of tests. This is partly caused by laboratory practices and partly by clinical staff practices.

For instance, the laboratory administration can take its share of the blame for its forcefulness in introducing admission profiles which add very little to patient care, the type of request form it uses which influences requesting patterns leading to waste and to an almost total lack of internal audit on services supplied.

Medical staff can be blamed for instance, for traditional practices of requesting tests which are never assessed or for their overreacting to current literature.

It is worthwhile repeating Krieg and La Combes' statement. They suggest that before ordering tests doctors should:

(i) Attempt to determine whether test sensitivity, specificity and predictive value are adequate to provide clinically useful information.

(ii) Ask themselves will the results of the tests change the diagnosis, prognosis or therapy.

(iii) Ask themselves will results of this test provide a better understanding of the disease process in this patient,

(iv) Ask themselves what they are looking for and why and will the patient benefit if they find it.

To these may be added from Wulff[23].

(i) Is there discomfort and risk to the patient?

(ii) What is the economic cost?

(iii) Is there data pollution (which he describes as "... results of unnecessary tests have a self-increasing effect as results of false positives lead to more tests."

Finally, Kreig[11] states "unless physicians regard the ordering of laboratory tests as a serious responsibility, worthy of the same thoughtful consideration as a history or physical examination, the privilege to select such services freely may not remain unrestricted in the future."

3. Quality or Quantity

It is quite apparent that the main emphasis over the years has been on a pathology service providing quantity at the expense of quality. Only comparatively recently has the service got to grips with the problem of quality. In some respects however, if present growth rates continue it will be increasingly difficult to ensure adequate quality. The unreasonable demands placed on this service by medical staff who are entirely ignorant of costs and the way in which the laboratory service operates will ensure this.

Further, if pathologists are to fulfil their proper role of interpretation of test results then there will need to be almost overnight a massive increase in their numbers. This is of course a pipe dream and in fact it is difficult to see that there will ever be sufficient pathologists to ensure a full interpretative service.

Some accepting the present situation see the introduction of the computer as a means of assisting in this area. There are developments with computer assistance in the recognition of disease patterns based on laboratory tests and other data. However, it is very difficult to see this as being more than something for the distant future when one considers the cost.

4. The Influence of the Medical School

It has been demonstrated that patients coming directly under the influence of teaching staff from the Medical School generally have

more tests carried out than patients without such influence. Further, the mere fact that the Medical School is in close proximity to hospital pathology services involves that service in trials and research projects which add to the rising workload.

One could easily argue that there is nothing fundamentally wrong with this practice. Indeed, where pathologists have both a service and an academic commitment, the division between service and research may become somewhat blurred. The sad fact is however that many projects once started never seem to come to an end and large numbers of test results become accumulated without being properly assessed. Also various trials and projects get started without any additional funding to pathology to cover costs and without prior consultation with laboratory administrators.

We are often led to believe that the division between service and research is difficult. Such statements are generally made by heads of departments with a foot in both academic and service camps. In fact the division between the two is not difficult and sooner or later rising workloads will dictate a course of action to separate them.

5, Blinded by Science

Least it be thought that this discussion is largely a criticism of medical staff and in particular the way in which they use the laboratory services, a word is spared here in their defence. Having been programmed through a lengthy course of basic sciences leading to clinical medicine the medical student is thrust into a hospital situation where he must satisfy his many peers and practice medicine using a vast array of diagnostic armamentaria. He has, during his training, undoubtedly been introduced to pathology, carried out some laboratory tests and been shown through a working laboratory. He has also been taught the value of the diagnostic processes. When he reaches the ward he will be shown a block of request forms and virtually given an open cheque to use them. He has no knowledge of the costs involved of laboratory tests, has little knowledge of precision limits—if a serum sodium which changes from 135 mmol/1 to 137 mmol/1 overnight is seen as significant it is repeated—has little concept of the chain of events which follow his marking a request form " urgent," and certainly is not taught the type of discrimination which has already been referred to in Kreig's and McCombe's statement.

By ticking appropriate boxes on a request form or using his own hieroglyphic abbreviations he will receive back an array of figures or even such meaningful statements as " specimen haemolysed " (which of course he knows has affected the potassium result) or even better a haematology report which may read " there is a marked neutrophil leucocytosis with a left shift in development. Mature forms appear to be hypersegmented. There is a significant polychromasia. The appearances are suggestive of a reactive state. Possibilities include acute blood loss, infection, inflammation, infarction, malignancy. The anaemia if not due to acute blood loss may be symptomatic of the disorders listed above. Neutrophil hypersegmentation can occur in infection, renal disease, megaloblastosis. Follow-up is suggested."

The sad fact is that practices learnt from this introduction to laboratory medicine find their way into private medical practice with resulting overuse of the laboratory services once again.

It is often said that any assistance to general practitioners which keep a patient out of hospital is justified. Essentially this is true but one cannot help but wonder how much of the $10.7 million spent in 1975/76 on private pathology really achieved this.

The time is long overdue for a shift in emphasis in the teaching of laboratory medicine to medical students.

6. What can be Done?

It may be deduced from what has been stated in this document that much of what the laboratory services do is unnecessary or wasteful and one may even question the very basis of the service. It must be clearly understood that laboratory testing when used correctly is a powerful tool in the diagnostic/management process and the main problems that have arisen are the results of certain practices developed by the laboratory and the users of the service. As Gitelman[7] states " Technological innovation and information overload may account for some dissatisfaction with the laboratory. The major factors producing dissatisfaction would appear to be

non-critical use of the laboratory in circumstances where the resolution of uncertainty is not scientifically possible or clinically indicated." If these are the main causes of unacceptable expansion of laboratory services, and it is considered that the situation needs to be brought back into control, this can only be achieved by a critical self-appraisal. There is no merit in sitting back and making such statements as "we are only responding to clinical demands" when in fact the type and extent of the service that is to be offered must be decided by the suppliers of the service and must be done within the constraints of available resources. It is a basic management principle that given a finite resource which basically means money, effective and efficient management of that resource is necessary to achieve the stated objectives. A corollary to this statement is that the managers must be in control of any outside influences which will make demands on those resources, otherwise the service is not able to be managed. It is suggested that this is exactly the situation in which the laboratory services at present find themselves. The service is not being managed properly either internally or externally.

To perpetuate the present situation is not only irresponsible but will eventually result in a downgrading of quality. This will be brought about by the lack of money. If one can read anything into public statements by Government Ministers and Hospital Board officials it is that a change in emphasis must take place away from technological aspects of medicine and the building of luxury hospitals. This policy, along with the present economic situation is affecting the funding of hospital boards which in turn will have ramifications right through all present hospital service areas. The time is ripe for houses to be put in order.

The following suggestion are made using this philosophy as a basis.

(a) *Expensive Laboratory Equipment*

Reference has already been made to the impact of multi-channel laboratory analysers. Guideline policies need developing in this area to avoid duplication and proliferation of expensive equipment. However, immediately one attempts to provide such guidelines a further set of problems arise. For instance, what is the policy on centralised, as opposed to decentralised services? Is equipment to be used on the continuous flow principle, with perhaps an automatic 20 tests per sample acceptable, or should one examine the growing number of fast, discrete analysers? What are the capital and running costs of equipment, etc? No attempt is made here to answer these difficult questions but it is suggested that there is a place for Central Government funding to permit the purchase and trial of equipment with a view towards national policies for the acceptance of certain types of laboratory equipment. Putting aside the question of costs which can only really be decided on a local trial basis, there is basic common sense in a return to the situation of requiring doctors to ask for certain tests that they require and to provide them with these results without the performance of a large number of unnecesssary tests. If national policies in this regard cannot be achieved then certainly some attempt should be made to assess equipment for a region or a large hospital board where there is more than one base hospital. Computerisation is also an important consideration. With most of today's modern equipment having built-in computer processors to control the instrument, the main problems revolve around handling the paper work. It is most unfortunate that the new Laboratory Core System for the Health Department Data-Processing Division is proceeding with an expensive and dubiously cost effective process control system utilising outmoded laboratory equipment. The first need in laboratories possessing this equipment is for new machines and not computerisation.

Arguments for the purchase of machines are sometimes cost-justified but often as not once the machine has been purchased, the arguments are not carried through. Three important points should be noted in this regard.

1. Where the cost justification for purchase is based on a reduction in staff, administrators should see in fact that there is a reduction in staff.
2. The machine will usually generate more work than done previously by manual methods. This usually results in some sort of a circular argument for laboratory administrators will then claim that more work is being done without an increase in staff.

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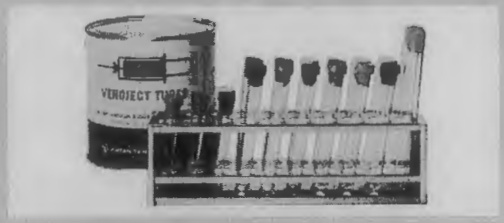

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3. The commitment to purchase the machine must also have the commitment to upgrade or replace the machine within a reasonable time span.

A final point in relation to the purchase of expensive laboratory equipment concerns the attempts to automate those areas which have traditionally been manual ones and in particular the areas of blood cell recognition and antibiotic susceptibility testing. There is, generally speaking, no real shortage of competent technical staff and provided the work load does not become over burdensome people are much more flexible and adaptive than machines. On this basis there seems little real argument to automate these and other traditionally manual areas.

(b) *Controlling the Workload*

It has already been pointed out that proper management of laboratory resources implies that the laboratory administration must have some control over external demands on its services. We tend to accept annual workload increases of about 20% or more without ever identifying the source of this increase. In other words, no audit systems operate and even where they do operate seldom are questions asked regarding the reasons or necessity for the increased testing. Provided a hospital has a reasonably steady state in terms of patient admissions and where no new outpatient services are started which produce a significant amount of laboratory work there is no reason why an increase in workload should take place. If it does, then the source of the increase should be identified and reasons for it sought.

Obtaining information on work-producing areas implies that some sort of information system is readily available. Such systems already exist in most hospitals but where they do not, a modest clerical effort could provide the information. Any additional costs in setting up this system could easily be supported by putting to use the information.

In other words, given a functioning laboratory the first aim in controlling the workload should be to establish an audit system to identify where the work is coming from. The aim should then be to regularly correlate this information with indices of hospital activity, e.g. admissions, outpatient attendances, etc. When a major discrepancy occurs, eg. significant workload increase with no extra admissions, questions should be asked. This should at least ensure that the workload level is held while other investigations are made.

The other investigations referred to are centred around a critical appraisal of traditional test requesting patterns. Two examples are given to illustrate the effectiveness of such investigations.

1. The Critical Care Unit of this hospital has a heavy routine laboratory testing programme for monitoring its patients. One such investigation is the daily performance of urinary electrolytes plus urine area, creatinine and protein. On investigation it was found that this routine was not an actual requirement but because it was simpler to give the nurse instructions to collect 24-hour urines each day instead of twice a week, the testing was done automatically.
2. A surgical ward had a routine pre-admission testing pattern involving haematology, biochemistry and a mid-stream urine for bacteriology. Upon admission the mid-stream urine was routinely collected and tested once again. There was found to be no good reason for this repeat of the urine test, it was simply a matter of lack of communication and the setting up of a routine practice.

There are undoubtedly many more such instances of routine wasteful practices.

The introduction of new tests also needs very close scrutiny. The earlier examples given of immunoglobulin estimations illustrates the need to control the introduction of new tests. In addition to these investigations medical staff should be made aware of the cost of laboratory tests. The provision of such information is a more difficult exercise. Nevertheless, if it is at all possible to provide wards with regular information and the cost of the laboratory requests, this should be done.

Throughout this section it has been implied that if information is available on the workload generated from different areas, action should be taken when a significant deviation occurs. Who should take action and what form should the action take? Pathologists are the people

to take action having been presented with the information. Failure to do so is irresponsible. The pathologist's major function is to interface between clinical staff and the laboratory. This is what their training is all about. Far too many of them, however, tend to bury themselves in the laboratory and fail to play an active role in this important area. Technologists can collect the information and highlight abuses but the final action rests with the pathologists. The form that this action should take is very much dependent upon the style of the pathologist. Information about service abuse may simply be released in letter form, regular costs per hospital area may be issued or meetings may be held with clinical staff. The main point however is that the pathologist must either be convinced that the additional work is justified or else he must take a firm line and bring the situation back under control.

Conclusion

This project started out to simply examine the requesting patterns for laboratory tests at Auckland Hospital. It has developed into a study of the workload assessment, the examination of factors responsible for the rising workload and a statement of suggestions for controlling the workload. The author firmly believes in the usefulness of the role of the laboratory in modern medicine but is equally certain that gross abuse and uncontrolled development of the service needs urgent attention.

" The age of hospital medicine, which from rise to fall has not lasted more than a century and a half, is coming to an end. The acute problems of manpower, money, access and control which beset hospitals everywhere can be interpreted as symptoms of a new crisis in the concept of disease." Illich[10].

Acknowledgments

I wish to thank the Medical Research Foundation for financial assistance. I am also indebted to Mrs Y. Cameron for her hard work in collecting much of the basic information, to the Management Services Research Unit of the Department of Health for helpful advice, to Dr S. E. Williams, " Pathologist Emeritus," for reading through the draft, to Dr Daylily Ooi, Pathology Registrar, Department of Clinical Chemistry, for assistance with case histories and to Dorothy for typing assistance.

Addendum

Since the writing of this report, several positive steps have been taken to rationalise the pathology services. For instance, admission profiling has been discarded as a policy, the request form for the Department of Clinical Chemistry has been reprinted to remove the large block testing concept and positive management has made hospital staff aware of laboratory costs. These changes have resulted in a significant lowering of the workload.

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Technical Communication

A Simple Inexpensive Record for Agar-gel Immunoelectrophoresis

One of the biggest disadvantages of Agar-gel Immunoelectrophoresis has been the problems involved in keeping a permanent record. Photography requires a suitable camera, illuminating frame, and access to facilities for film processing; drying the gel on the supporting glass plate necessitates a continuous supply of plates, which are unwieldy, difficult to file, and easily broken. An alternative technique has been developed in which the gel is dried on to a piece of x-ray film, the thin flexible support then allows easy handling and storage. The technique for preparing such plates is described below.

Material and Method:

1. Preparation of the film: To remove the emulsion from exposed x-ray film it is placed in sodium hydroxide (5N), gently heated on a hot plate to 65° and allowed to stand for two hours. The softened emulsion is washed from the film with running tap water and the film returned to sodium hydroxide (5N) at room temperature overnight. The remaining emulsion is then removed with tap water. Finally the film is rinsed with distilled water and air dried. It is then trimmed to size, approximately 1cm smaller than the glass supporting plate, and stored until required. If the temperature of the sodium hydroxide is increased above 65° it enhances the efficiency of emulsion removal but may cause the film to buckle thereby rendering it useless. Significant reduction in temperature reduces the efficiency of the process.

2. Preparation of Agar plates: The glass plates are cleaned in the usual manner, 1 to 2 drops of agar solution are placed on the plate and the x-ray film put on top. Air bubbles and excess agar are removed by wiping with a soft tissue and the film is positioned in the middle of the glass plate. This process "fixes" the film and prevents it floating when the agar-gel electrophoresis layer is poured. A measured volume of agar solution is then poured on to the prepared plate as for standard agar-gel electrophoresis. Wells and troughs can be cut in the agar layer as desired. A diagrammatic view of a prepared plate is shown in Figure 1.

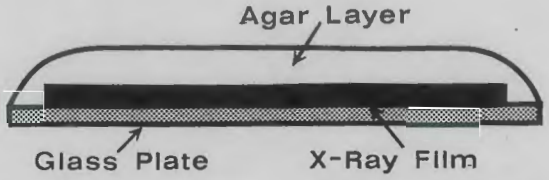

Figure 1. Diagrammatic representation of the cross section of a prepared agar-gel electrophoresis plate.

3. Preparation of a permanent record: Electrophoresis, diffusion, washing, drying, and staining are performed as usual. Glycerol (75ml per litre) is added to the destaining solution. This prevents the agar-gel shrinking, and peeling off the film when it is finally dried. The film is removed from the glass plate during destaining by running a scalpel blade around the edge of the film. It will then float or lift off. After destaining the film is allowed to drain and air dry. For more rapid results it may be exposed to a flow of warm, not hot, air. If there is a slight excess of glycerol it can be removed from the film and gel surface by gently wiping with a wet tissue.

The processed gel, when completely dry, can be sellotaped into a workbook, filed or stored as required. It is always available for reassessment and can easily be photographed should it be needed for publication.

A. M. Buchanan, J. E. Coyte
and C. W. Small,
Chemical Pathology Department,
Green Lane Hospital.

January 1977.

Friends of the Institute

DR STEPHEN WILLIAMS

Dr Stephen Williams, Head of the Auckland School of Medical Laboratory Technology and Pathologist-in-Charge of the Cytology Laboratory at National Women's Hospital. Dr Williams retired from the hospital service in October 1976.

His professional career was at all times distinguished. He was on active service in the Pacific during the Second World War and on his return to New Zealand in 1951 was appointed to the position of Pathologist-in-Charge at Green Lane Hospital. During the next nine years he was closely associated with the fascinating developments in heart surgery at that hospital. In 1960 he was appointed Director of Laboratory Services for the Auckland Hospital Board. He established the Auckland School of Medical Laboratory Technology and actively encouraged teaching programmes. He came to the realisation over the next several years that this demanding position was too much for one man and in 1969 he resigned from the Directorate in favour of an Advisory Committee of Pathologists upon which he served until he retired.

Following his resignation from Director of Laboratory Services, he was appointed to the joint positions of Head of the Medical Cytology Laboratory at National Women's Hospital and Head of the Auckland Hospital Board's School of Medical Laboratory Technology, positions he held until his retirement.

Dr Stephen Williams' innovations and activities in pathology, and in particular, medical cytology, are too numerous to list, but in particular his involvement with the introduction of examinations for laboratory assistants and his founding of the New Zealand Society of Cytology and election to its first presidency are worthy of note. It was however, his consuming interests in medical laboratory workers and their education and welfare that we, as an institute, owe to him much of what has been achieved in the education area today. He has been in the forefront of efforts made over the years to enhance the educational and professional status of the medical laboratory technologist.

His wisdom and steadying influence will be sorely missed in this rapidly changing world. We wish him well. IMC.

Friends of the Institute

DR DENIS T. STEWART

Chairman, Pathology Services,
North Canterbury Hospital Board,
Associate Professor of Pathology.

It was with many regrets that Dr Stewart was farewelled upon his retirement on August 3, 1976, at an afternoon tea for the whole Pathology Services staff, held in his Anatomical Pathology Museum, where he was presented with a cheque and a book of Russell Clark's paintings.

He joined the staff of the Pathology Department, Christchurch Hospital, in 1939 as the Assistant Pathologist, after lecturing in anatomy at the Medical School, Dunedin, for two years. He has always been very hard working and pleasantly enthusiastic and he very shortly established a blood bank.

Early in 1940, he left with the 2nd Echelon as Pathologist to 1 N.Z. General Hospital in Greece. When the hospital was transferred to Egypt, he set up the 1st N.Z. Mobile Transfusion Unit which he took into the desert during the battle of El Alamein in 1942. He returned as a major and in 1944, took INZGH to Italy, being the Chief Pathologist to 2 NZEF.

Over the years, Dr Stewart has introduced many innovations to the laboratory and his knowledge and interests have been wide. In 1950 he arranged with the Board for the Department to be divided into units with a pathologist in charge of each. In 1972 these units were made into autonomous departments within the newly named Pathology Services, covering all the Board's hospitals and these departments are now enlarged beyond recognition by former staff.

During all his career, Dr Stewart has maintained a very active interest in the education and status of technologists. He was a member of the Laboratory Workers Salaries Grading Committee for some years and has always put a great deal of work into attempting to have salaries upgraded for his staff.

As supervising pathologist to the Ashburton, Greymouth and Westland Hospital Boards, he has often been helpful in arranging training periods in our laboratory for both medical and technical staff from their laboratories.

He has been an examiner for the Health Department examinations and has enthusiastically encouraged teaching in all its aspects to trainees and to all laboratory staff. He has personally conducted a series of Clinico/Pathological meetings for senior technologists on many occasions.

His honesty and hard work is perhaps exemplified in his suggestion to our 1953 Conference, that a medical laboratory worker's motto might be "near enough is not good enough." DHA.

Tetrabromphenol Blue — Assessment of Albumin Specificity

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Received for Publication, June, 1977.

Introduction

The binding of acidic dyes and other negatively charged ions is regarded as a specific property of the albumin fractions when determining albumin in blood. Sorensen[4] first described the use of the azo group of indicators for the determination of proteins in 1909 and a commercial 'dipstix' is produced using tetrabromphenol blue — R as its indicator (Albustix, Ames Company), both techniques using the Protein Error of Indicators concept. When methods of assessing specificity of techniques for the measurement of albumin are described, to date, all have used albumin and gamma globulin. In this paper the reaction of albumin, transferrin and gamma globulin with 3', 3', 5', 5'—Tetrabromphenol—sulphonphthalein (tetrabromphenol blue) is assessed.

Material and Methods

Human albumin and transferrin were obtained from Hoescht (N.Z.) Ltd and human gamma globulin fraction II was obtained from the Sigma Chemical Corporation, St Louis, USA. To assess the reactivity of the three proteins to tetrabromphenol blue, the method of Hemmingsen[1] was used.

All spectrophotometer readings were made using a Pye Unicam SP1800 recording spectrophotometer. Reaction mixture pH values were measured using a Radiometer PHM 28 pH meter.

Standards

Stock standards each containing 50g/litre of the respective proteins were prepared in both isotonic saline and distilled water. Dilutions were made of each standard to correspond to 1, 2, 3, 4, and 5g/litre of the respective protein.

Results

a. Absorption Spectra

An absorption spectrum of the reagent blank revealed two peaks at 420nm and 597nm in both the isotonic saline and distilled water blanks. However, when any one of the three proteins was added to the tetrabromphenol blue reagent, the absorption peak at 597 shifted to 610nm; the 420nm peak remained unchanged.

b. Protein Reactivity

The degree of reactivity of the three proteins in both saline and distilled water, is shown in Table I.

c. Alteration of pH

The saline and distilled water 5g/ litre standards of the three proteins were read at minute intervals for 15 minutes. No change from the initial pH values of 2.82 for the proteins in water and 2.80 for the proteins in saline were observed.

Discussion

Previous studies have shown that acidic dyes were specific for albumin [1, 2, 3]. In this paper

TABLE I

	Isotonic Saline			Distilled Water		
g/litre	Albumin	Transferrin	Gamma Globulin	Albumin	Transferrin	Gamma Globulin
0	0.12	0.12	0.12	0.12	0.13	0.12
1	0.22	0.23	0.12	0.21	0.24	0.12
2	0.31	0.27	0.12	0.29	0.26	0.12
3	0.36	0.29	0.12	0.34	0.29	0.12
4	0.39	0.30	0.12	0.37	0.30	0.12
5	0.42	0.31	0.12	0.40	0.30	0.12

Optical densities of albumin, transferrin and gamma globulin standards in isotonic saline and distilled water.

internal standard. Paracetamol powder was obtained from H. F. Stevens Ltd.

Method

To 200 μl of the plasma samples in a 10ml screw capped test tube add 200 μl of internal standard (aqueous N-butyryl-p-aminophenol 600 μmol/l), 5ml of ethyl ether, an about 500mg of sodium chloride. Treat a 200 μl sample of a standard solution of paracetamol (1 mmol/l, aqueous) in the same manner. Roll the tubes for 10 minutes on a multi axle rotator, then centrifuge briefly. Transfer the ether layer to a 10ml test tube containing about 500mg anhydrous sodium sulphate, shake, then centrifuge briefly. Decant the ether layer into a 25ml pear shaped flask containing 50 μl acetic anhydride. Remove the ether using a rotary evaporator. Prior to sampling for GLC analysis, add 100 μl of methanol to the flask. Inject a 1 μl sample into the GLC. The derivatised paracetamol has a retention time of 0.75 relative to the internal standard (fig. 1). Plasma paracetamol levels are determined by comparing the ratio of the paracetamol and internal standard peak heights in the test, with the ratio in the standard.

Results

The method is linear over the range of clinical importance in overdose cases (0.01-2.5 mmol/l). Ten analyses of a plasma solution containing 600 μmol/l paracetamol gave a mean result of 593 μmol/l with a standard deviation of 15 μmol/l.

Discussion

Derivatisation was found to be complete in less than 10 seconds. No peaks corresponding to unchanged paracetamol were seen in chromatograms obtained by injecting samples from solutions of paracetamol in acetic anhydride taken immediately after the solvent was added. Repeated injection of acetic anhydride caused some deterioration of the column. This effect was lessened by adding excess methanol to the acetic anhydride residue, to give methyl acetate.

Other drugs commonly present in preparations containing paracetamol were found not to interfere with the analysis. The use of the alkali flame ionisation detector is not essential to the method, but by enhancing the signal due to the paracetamol and N-butyryl-p-aminophenol relative to non-nitrogenous contaminants and the solvent, it enables the chromatogram to be run more quickly.

Figure 1: Chromatogram of plasma containing 500 μmol/l paracetamol. Peak A = paracetamol. Peak B = N-butyryl-p-aminophenol.

Conclusion

Paracetamol is normally a safe drug when taken in therapeutic quantities. However, when large overdoses are taken severe liver damage can occur. Given the time of ingestion, the likelihood of an overdose being hepatotoxic can be determined from the plasma paracetamol level using the curve derived by Prescott et al[4]. Appropriate therapy can then be undertaken if considered necessary [1, 4]. To be useful in these circumstances an analytical method for determining plasma paracetamol

levels must be rapid, and accurate over the range of interest. The method described meets these criteria.

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Sequential Dialysis on the Technicon SMA 6/60 (4+2)

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Department of Laboratory Services, Division of Biochemistry, Wellington Hospital.

From a paper read at Conference, Queenstown, 1977

Introduction

Sequential dialysis by recycling the waste of each dialyser into the next one, plus the use of a common sample diluent, has reduced our sample size from 0.88ml to 0.39ml. This modification has resulted in the decreased use of pump tubes, reagents, calibrating and quality control sera; while maintaining precision and linearity.

Materials and Methods

The change made on the SMA 6/60 was the introduction of plastic tubing connection to carry the waste of the sodium—potassium dialyser into the carbon dioxide, chloride and finally the urea dialyser. The creatinine channel retained its own sample and diluent lines. The carbon dioxide diluent phasing coil was replaced by a recipient coil just before the reagent enters the colorimeter in order to keep the phasing of the other channels independent of the carbon dioxide channel. The creatinine flowcell was changed from 1.5mm to 2.0mm. All the sample lines, other than that of the sodium-potassium channel were disconnected and removed including their diluent and airlines. The remaining pump tubes were then relocated on to one Auto Analyzer pump.

All the methodologies for the sodium, potassium, chloride, carbon dioxide, urea and creatinine channels are according to standard Technicon methodologies. Originally the acid lithium sulphate was used as the sample diluent (except for creatinine). It was found by estimating lithium levels of the diluent before and after dialysis that only 1.0% of the lithium dialysed across the membrane. It was then decided to use 0.25 N H_2SO_4 as the sample diluent and 1/100th the original lithium sulphate concentration (0.137 g/L) on the recipient side of the sodium-potassium dialyser. Figure 1 shows the modified manifold flow diagram.

Results and Discussion

Table 1 shows the precision and carryover of the modified manifold. Reduction of sample size on the SMA 6/60 (4 + 2) by sequential

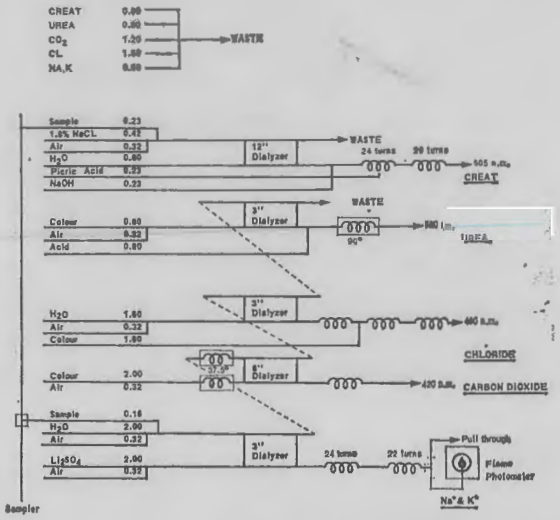

Figure 1: Modified Manifold Flow Diagram 6/60 (Line size in ml/min)

Table 1.

Within Batch Precision

Test	Mean mmol/l	N	C.V. %
Sodium	148	40	0.35
Potassium	5.4	40	0.93
Chloride	108	40	0.68
Carbon Dioxide	19	40	1.05
Urea	32.2	40	0.75
Creatinine	0.37	40	1.25

Carryover

Test	%
Sodium	1.2
Potassium	1.4
Chloride	1.1
Carbon Dioxide	1.6
Urea	0.9
Creatinine	1.2

Between Batch Precision

Test	Mean mmol/l	C.V. %	Mean mmol/l	C.V. %	Mean mmol/l	C.V. %	N.
Sodium	136	0.93	148	0.85	129	1.05	31
Potassium	4.5	1.92	5.3	1.65	3.8	2.06	31
Chloride	91	1.45	105	1.10	84	1.57	31
Carbon Dioxide	19	5.5	24	4.3	19	5.3	31
Urea	8.1	2.05	30.4	1.76	14.9	1.90	31
Creatinine	0.19	2.7	0.29	2.25	0.66	2.0	31

dialysis was described and introduced by Shihabi. Their manifold differs from ours in that we have a creatinine channel to their glucose channel. Because creatinine needs sodium chloride to facilitate dialysis across the membrane, this channel had to retain its own sample line and saline diluent. In order to reduce the sample size to this channel a 2.0mm instead of 1.5mm flowcell was fitted into the colorimeter. The linearity of the six tests measured on the modified manifold did not differ from that of the original manifold. Although increased air bubble breakage occurs as the sample passes through four dialysers this did not significantly introduce increased recorder noise or necessitate more frequent phasing. The modified manifold has the following advantages

1. Only 26 pump tubes instead of 36 are used.
2. The number of reagents used is reduced from 15 to 10.
3. The need of only one pump instead of two pumps. This releases a spare pump which can be set up in duplicate for a quick pump tube changeover.
4. The use and cost of calibrating and quality control sera is cut by 50%. In our laboratory this approximates $2,500 per year.
5. Patients sample size is reduced permitting paediatric samples to be processed and permits the use of 5ml size vacutainers.

Acknowledgments

The author wishes to thank Mr J. Newton for advice and help, and Mrs M. Pyett for typing the manuscript.

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See also Powell, J. C. Modification to the SMA 12/60 to Enhance Productivity. (1977), N.Z. J. med. Lab. Technol. **31**, 30. — *Editor.*

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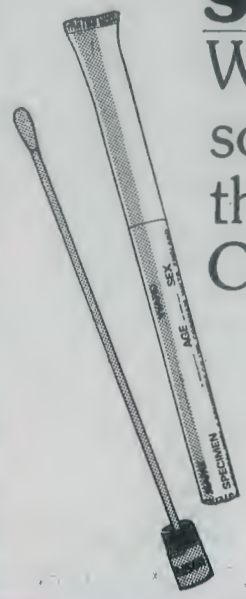

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Comparison of the Minitek System with Routine Laboratory Methods for the Identification of Enterobacteriaceae

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Received for publication, May, 1977.

Abstract

The Minitek System (BBL) was compared with our routine method for identification of Enterobacteriaceae. This system identified 95.8% of the 193 organisms tested. The method is therefore sufficiently accurate for general use in a clinical laboratory.

Introduction

The use of commercially prepared systems for the identification of Enterobacteriaceae is increasing. These systems provide all the materials for the commonly used tests in a simplified form. However, improvements in convenience should not compromise the accuracy of identification. This paper describes a study undertaken to compare the accuracy of the Minitek system (BBL) with standard methods of identification in a diagnostic laboratory.

Material and Methods

The 193 bacterial strains examined were fresh isolates obtained from clinical specimens sent to the diagnostic laboratory. All specimens were initially plated on to horse blood agar (5% horse blood in Columbia agar base), MacConkey agar, Robertson's Cooked Meat Medium (for those specimens cultured anaerobically) and CLED media for urine specimens.

For the identification of Gram negative bacilli, one colony from the MacConkey plate was stabbed with a straight wire and emulsified in the BBL inoculum broth which was mixed thoroughly on a Vortex mixer. This broth was used to inoculate both the routine media and the Minitek system.

The routine method for the identification of Enterobacteriaceae consisted of inoculating ONPG-peptone broth which was incubated for 4 hours. ONPG positive organisms were then subcultured on TSI agar, phenylalanine agar slopes, O-F (dextrose) medium and MacConkey agar. The test for Indole production was performed on the ONPG-peptone broth after overnight incubation using Kovack's reagent. Additional carbohydrate fermentation tests were performed on any culture which could not be identified by these routine tests. All reactions were read after overnight growth at 37°C.

Minitek System

The Minitek system consists of a covered, rectangular plastic plate containing 12 wells, a multiple disc dispenser, a pipetter with disdospable tips, bottles containing 1.0 ml inoculum broth and a humidor to hold the plates while incubating. The plastic plate was placed in the dispenser and preselected discs were dispensed into the wells. In this study the following discs were used. For lactose fermenting organisms: dextrose-nitrate, indole-H_2S, hydrogen sulphide, ornithine decarboxylase, citrate, Voges-Proskauer. For non-lactose fermenting organisms these additional substrates were used: ONPG, urea, phenylalanine, sucrose. The wells containing indole-hydrogen sulphide, urea, ornithine, decarboxylase, discs were covered with 0.5 ml Ondina Oil (Shell) after inoculation.

To inoculate 0.5 ml of the inoculum broth was dispensed into each well using the pipetter. The lid was replaced and the plate placed in the humidor and incubated overnight at 37°C.

The results for each method were read and recorded separately by two independent observers. Reactions were recorded as correct if they agreed with our routine test.

Results

One hundred and ninety-three organisms were tested in parallel. The results for each genus are shown in Table 1.

Table I: Results of organisms tested by both methods.

	Total isolates	Minitek identified	Correctly identified
			(%)
E. coli	68	63	92.6
Klebsiella	53	51	96.2
Enterobacter	7	6	85.7
Pr. mirabilis	22	22	100.0
Proteus sp.	2	2	100.0
Pseudomonas	36	36	100.0
Acinetobacter	5	5	100.0

Fourteen tests were incorrect when compared with our routine methods. The overall correlation for all substrates was 98.8% Table 2.

Table II: Results of individual tests with Minitek system and routine system.

	Number of tests	Number incorrect	Correlation with routine test
			(%)
Dextrose	193	0	100.0
Indole	193	1	99.5
H_2S	193	3	98.5
Ornithine decarboxylase	193	2	98.9
Citrate	193	0	100.0
ONPG	193	0	100.0
Urea	83	5	93.9
PPA	83	0	100.0
Sucrose	83	0	100.0
VP	193	3	98.5

With the H_2S disc test three were positive with the Minitek but negative by our routine method. Repetition of these tests gave the same result. These false positive reactions made identification impossible in these three instances (Table 2).

With the urea disc some difficulty was experienced in deciding if the test was negative when only a slight change in colour occurred. Although the urease reaction was not tested on ONPG positive organisms with our routine methods, four strains of *Escherichia coli* which were lactose negative were urease positive by the Minitek and when tested by our urea media were negative. These four organisms were unidentifiable by the Minitek system. One strain of *Proteus mirabilis* was urea negative by the Minitek but urea positive by the routine test but this result did not cause misidentification.

No difficulty was experienced in reading the sugar fermentation reactions as strong positive reactions occurred with all these discs. The citrate disc was only read as a positive reaction if there was a definite blue colour. Using this criterion a 100% correlation was observed with this test.

We found that the Minitek Voges-Proskauer reaction was more sensitive than our routine method for in three cases the Minitek VP was positive and the routine method negative. However, these results did not affect the identification of the organism.

Two incorrect results with the Minitek ornithine decarboxylase disc and one incorrect indole reaction were recorded but only one of those results affected the identification of the organism (ornithine decarboxylase of a *Klebsiella* — Table 3).

Table III: Organisms misidentified by Minitek system.

Routine identification		Minitek identification	Minitest	Routine
E. coli	1	Citrobacter	Indole—	+
	4	Unidentifiable	Urea+	—
Klebsiella	2	Unidentifiable	H_2S+	—
			Ornithine+	—
Enterobacter	1	Unidentifiable	H_2S+	—

Paraffin oil as recommended by the manufacturers was unsatisfactory because it was difficult to dispense. However, substituting Ondina Oil (Shell) was a vast improvement and no difficulty was encountered with it. The time before the oil was overlayed was important. A delay of more than 15 minutes did give false results.

Inadequate mixing of the inoculum broth was associated with poor growth and we found that using a Vortex mixer eliminated this problem.

Because the Minitek pipetter broke, two drops from calibrated Pasteur pipettes delivering approximately 0.025 ml per drop were substituted. No differences were observed when the substitute was used. Indeed, some users preferred them to the Minitek pipettes.

Discussion

The Minitek system has the advantage of speed, flexibility, ease in interpretation and

an acceptable level of reliability, together with a considerable saving in laboratory space. The overall accuracy of the Minitek system for identification in this survey was 95.8% which confirms the findings of other workers[1, 2, 3] who found a similar level of correlation. We support their conclusions that it provides a very satisfactory method for routine identification of Enterobacteriaceae.

The false positive hydrogen sulphide reactions were a serious disadvantage and this reaction was responsible for three of our false identifications in this survey. This finding has been reported by other workers[2, 3].

As with Kiehn *et al.* (1974)[2] we agree that delay in adding the oil seal is responsible for incorrect results. Careful attention to this resulted in elimination of this error.

The Minitek pipetter was disappointing. It did not stand up to the continual use in our laboratory. Calibrated Pasteur pipettes which can be re-used and are cheaper than the Minitek pipettes were found to be an acceptable alternative and did not affect the reliability or sensitivities of the test.

Our results indicate that the Minitek system has a place in a diagnostic laboratory where it can provide a simple and reliable alternative method for identification of the Enterobacteriaceae.

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Abstracts

Contributors: E. R. Crutch, Shirley Gainsford, J. Hannan, L. M. Milligan and Janice Parker.

Clinical Biochemistry

The Significance of Human Chorionic Gonadotropin in Blood Serum for the Early Diagnosis of Ectopic Pregnancy. Milwidsky, A. *et al.* (1977), *Acta Obstet. Gynec. Scand.* **56,** 19.

The urine immunological pregnancy test is not satisfactory for early diagnosis of ectopic pregnancy because of its low limit of sensitivity (700 IU/l), resulting in an accuracy of 50-87.5% in this type of case. The diagnosis of a very early or a pathologic pregnancy can thus be missed. Using a double antibody radioimmunoassay technique (kit from Sorino—Italy), of 23 women with suspected ectopic pregnancy, in all cases (14) of ectopic pregnancy, chorionic gonadotropin values in the serum ranged from 182-884 mIU/l, while in the remaining 9 cases, without ectopic pregnancy, the range was 9.1-56.0 mIL/l. It is concluded that measurement of chorionic gonadotropin in serum by the radioimmunoassay technique is an important tool in the early diagnosis of ectopic pregnancy.

—J.H.

Excretion of Liver Antigens in the Urine of Patients with Hepatic Diseases. Boss, J. H. *et al.* (1976), *Res. in Exp. Med.,* **167,** 51.

Liver antigens were detected by double immunodiffusion in the urine of 4/42 patients with various liver diseases. The presence of hepatic antigens in the urine did not correlate with severity of jaundice nor SGOT levels but did correlate with parenchymal necrosis and was associated with a high mortality. Use of more sensitive techniques, *e.g.* radioimmunoassay and examination of urine samples at frequent intervals would facilitate the detection of liver antigens. —J.H.

An Audio Urine-Glucose Analyser for Blind Diabetics. May, J., Inman, S., Wilcox, D. E. and Beckett, R. S. (1977), *Diabetes,* **26,** 192.

Based on the surface reflectivity of Diastix strips (Ames), audible pulses are counted and the glucose level thereby deduced. J.H.

Use of Equilibrated Blood for Internal Blood-Gas Quality Control. Leary, E. T., Delaney, C. J. and Kenny, M. A. (1977), *Clin. Chem.* **23,** 493.

This paper summarises the authors' observations on tonometry and blood-gas quality control during the past six years. They find equilibrated blood to be a sensitive, inexpensive, reproducibly prepared, and reasonably stable control matrix providing a necessary and extensive control of blood gas analysis. —J.P.

Enzymatic Determination of Cholesterol and Triglyceride with the Abbott Bichromatic Analyser. Barbour, H. M. (1977), *Ann. clin. Biochem.* **14,** 22.

Enzymatic methods for cholesterol and triglycerides on the Abbott Bichromatic Analyser are compared with standard non-enzymatic assays involving solvent extraction and the use of corrosive liquids. Factors

affecting the performance of the A.B.A. 100 and precision of the enzymatic assays on this instrument are discussed. —J.P.

Paracetamol Estimation: Comparison of a Quick Colorimetric Method with a Standard Spectrophotometric Method. Weiner, K. (1977), *Ann. clin. Biochem.* **14,** 55.

A new colorimetric method for the estimation of plasma paracetamol has been slightly modified and compared with a standard spectrophotometric method. Precision, accuracy, and recovery by the colorimetric method proved acceptable although the sensitivity was considerably lower than that of the spectrophotometric method. The method is quick and easy to perform and particularly recommended for cases of suspected overdose. —J.P.

Evaluation of Automated Glucose Oxidase Methods for Serum Glucose: Comparison to Hexokinase of a Colorimetric and an Electrometric Method. Koch, R. and Nipper, H. C. (1977), *Clin. Chim. Acta.* **78,** 315.

Two automated glucose oxidase methods are evaluated with respect to accuracy, precision, recovery, linearity and potential interference, and on the results obtained are both highly recommended for routine use in the clinical laboratory. The methods are Trinder's method on an Autoanalyser II and the Beckman System I glucose method using a Clark-type oxygen electrode.

—J.P.

Haematology

Improved Electroimmunoassay of Factor VIII-Related Antigen Chute, Ann, Haddow, J. E. and Ritchie, R. F. (1977), *Clin. Chem.* **23,** 602.

Factor VIII-related antigen migrates poorly into gel during electrophoresis in agarose, probably in part because of the relatively high sulphate content of the commonly used agars. The use of low sulphate agar gives rise to rockets with higher amplitude, sharply defined, which are easily measured and translated into a standard curve that has a steeper slope, which allows for greater accuracy within the usual testing range. —E.R.C.

Detection of Factor VIII Inhibitors with the Partial Thromboplastin Time. Lossing, T. S., Kasper, C. K. and Feinstein, D. I. (1977), *Blood,* **49,** 793.

An easy, sensitive screening test using the PTT can detect even very low titre factor VIII inhibitors. When a patient-normal plasma ratio of 4:1 was used, and that mixture was incubated with kaol in-cephalin suspension for 2 hours at 37°C, all of the inhibitors in the study were detectable, including some very weak inhibitors with titres of 0.1, 0.3 and 0.4 Bethesda units. —E.R.C.

Development & Description of the "Random Duplicates" Method of Quality Control for a Haematology Laboratory. Carstairs, K. C., Peters, Eren, & Kuzin, Elizabeth J. (1977), *Am. J. clin. Pathol.,* **67,** 379.

This paper discusses the development of the "Random Duplicate" method of quality control, especially pertaining to haemoglobin values and white cell counts performed on a Coulter Model "S". Included in this paper is a protocol for daily set-up procedures, daily shut-down procedures and preventive maintenance of the Coulter Model "S". —E.R.C.

Variation Among Commercial Activated Partial Thromboplastin Time Reagents in Response to Heparin. Shapiro, G. A., Huntzinger, S. W., and Wilson, J. E. (1977), *Am. J. clin. Pathol.* **67,** 477.

The activated partial thromboplastin time (APTT) has been advocated for monitoring heparin effect. This paper details a study comparing the sensitivity of commercially available APTT reagents. The authors conclude that the efficacy of a commercial automated APTT reagent in heparin management remains to be established. —E.R.C.

Rapid Screening for Lupus Erythematosus Cells Using Cytocentrifuge-prepared Buffy Coat Monolayers. Garnett, R. F., Atkinson, Barbara F., Bonner, H. and Wurzel, H. A. (1977), *Am. J. clin. Pathol.* **67,** 537.

Cytocentrifugation is a useful technique to concentrate and adhere cells from body fluids directly on to a small area of a glass slide without significant morphologic distortion. The Shandon-Elliott cytocentrifuge is used by the authors to prepare buffy coat monolayers for the rapid screening of LE cells. The area to be screened is significantly decreased and the morphologic features of the LE cells are well preserved. Technologist screening time was reduced by about 50% . —E.R.C.

Quality Control in the Microbiological Serum Folate Assay. Aird, Alice, Carter, R. H. and Rush, B. (1977), *Pathology* **9,** 199.

Low values obtained in the microbiological assay of serum folate are often due to the presence of antibiotics in the test serum. The assay has been modified to permit consistent recognition of the presence and extent of such contamination. Other assay variables have been investigated and a quality control system devised which rapidly identifies the presence of inconsistencies in any one assay batch. The system further allows for the reporting of some clinically useful results from an imperfect assay batch, thus reducing the necessity for re-assay of some test sera. —E.R.C.

A Simple Method for the Separate Measurement of Transcobalamins I, II and III Normal Ranges in Serum and Plasma in Men and Women. Jacob, Elizabeth, Wong, Kit-Tai J. and Herbert, V. (1977), *J. Lab. clin. Med.* **89,** 1145.

The method involves batch separation of transcobalamin (TC) I and III from TC II by means

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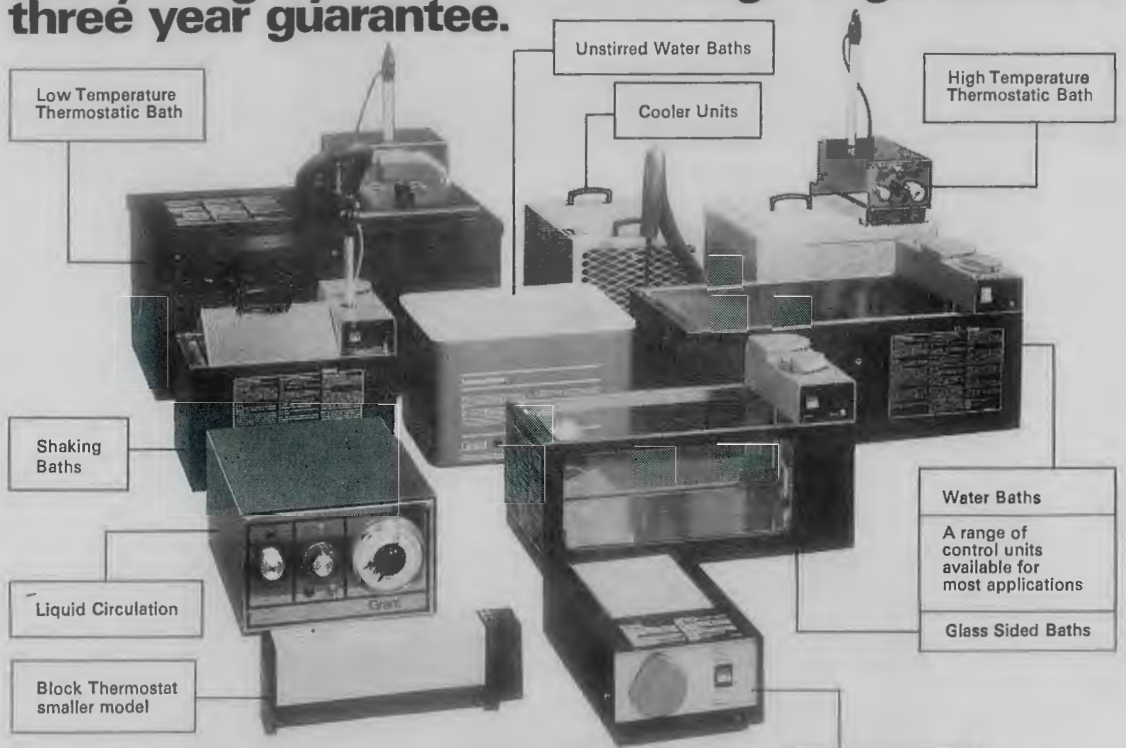

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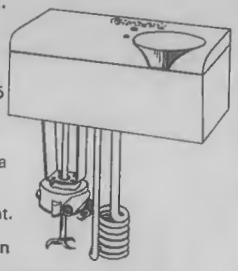

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Routine Laboratory Assessment of Postoperative Chest Infection: A Perspective Study. Wilkinson, P. J., Ball, A. J., Doran, J., Gillespie, W. A. and Orton, Vivian S. (1977), *J. clin. Path.* **30**, 417.

A study of standard laboratory methods for sputum examination was made on postoperative patients and the clinical significance of the culture results was assessed. It was found that homogenisation and dilution of sputum had no advantage over direct culture when selective medium for haemophilus, together with a non-selective medium such as blood agar was used. In most cases clinical evidence of chest infections was associated with profuse growth of pneumococci or haemophilus whilst *Staph. aureus* and other gram negative bacilli were mainly isolated after antibiotic therapy.

—S.G.

A New Method for Antibiotic Assay Based on Measurement of Bacterial Adenosine Triphosphate Using the Firefly Bioluminescence System. Harber, M. J. and Asscher, A. W. (1977), *J. Antimicrob. Chemother.*, **3**, 35.

In two surveys of the accuracy of gentamicin assay techniques, Reeves (1974) showed that approximately 80% of the laboratories sampled produced results which were either poor or highly misleading. As most of these laboratories (70%) used a plate diffusion method, it is clear that a more reliable type of assay is desirable for routine use in hospital laboratories. Presented in this study is a technique which utilises relatively simple equipment for the rapid assay of gentamicin and other antibiotics in serum.

—J.H.

Book Reviews

Theory and Practice of Histological Techniques. Edited by J. D. Bancroft and A. Stevens. 436 pages. Illustrated. Published by Churchill Livingstone 1977. Cost $NZ35.05. Obtainable from N. M. Peryer Ltd., Christchurch.

The book consists basically of 24 chapters by 18 contributors covering the spectrum of histological techniques from microscopy, fixation and tissue processing through to enzyme histochemistry. Most chapters are followed by extensive references.

I found it a very stimulating and readable book which one could open at random and immediately become immersed in whatever subject was being discussed. A glance down the "List of Contributors" shows that nearly all the authors are or have been lecturers at a college or medical school — this probably explains the excellent presentation of the text and the depth of knowledge of the contributors.

The basic theory of light, phase, interference and U.V. microscopy is explained lucidly, although a few photographs of properly and badly adjusted microscopes would give added understanding. A new system of classifying fixatives is proposed and the complexity of the mechanism of fixation along with the variants that can be applied to alter the effects of fixatives is discussed in detail. Following routine paraffin processing by manual and automatic methods the authors of this particular chapter present interesting alternative waxes resins and double embedding techniques. The knife sharpening section covers the range of types of microtome knives along with the wide variety of abrasives one can use, although only one automatic sharpener is described. Perhaps one day someone will review the whole range of automatic sharpeners available, even if only for the sake of posterity. Microtomy is adequately explained and an extensive table covers faults and their remedy.

Separate chapters cover connective tissues, protein, amyloid, carbohydrates, lipids, pigments, micro-organisms, bone sectioning techniques, neuropathological techniques, special tissues and enzyme histochemistry. The technical methods dispersed throughout the chapters fall naturally into the description and discussion of the various subjects.

Exfoliative cytology is discussed in a short chapter, which although concise and useful, cannot possibly do full justice to such a subject, which is a specialty of its own.

Electron microscopy preparation techniques are well covered and as a sign of the times, quick embedding techniques for biopsy materials are given.

The chapter describing museum techniques is fairly short, but contains precise details of mounting specimens and constructing perspex jars and embedding photographs and x-rays.

I enjoyed reading this book. I like the way it is set out with the techniques distributed amongst the discussion, its largish size, 250 mm x 190 mm x 30 mm, and smallish print ensure that it is packed with interesting and useful information. I recommend the book to anyone taking a part II, or more especially a part III, histology examination and also any Histotechnologist or Pathologist wishing to know

the techniques available in order to extract the maximum amount of information from surgical material.

D. Tingle.

Basic Laboratory Procedures in Diagnostic Virology. Mary Christensen, M.S., Ph.D. Published Charles C. Thomas, Illinois 1977. 115 pages. Plastic covers and spirally bound. $US9.75.

The preface emphasises that ". . . this manual is meant primarily as a guide for the most frequently used routine methods carried out in a virus diagnostic laboratory." For this reason methods such as animal and egg inoculation are not discussed and the rubella-haemagglutination-inhibition test is omitted as being an exacting test for experienced personnel only.

With this in mind the subject is dealt with in two parts. The first, entitled Virus Isolation and Identification for the Diagnosis of Viral Infections, gives an excellent introduction for the uninitiated into the basic properties and major groups of animal viruses, and the principal techniques involved in viral isolation. A rather complicated system of filing is then described which would be unwieldy for a smaller laboratory to manage. The next section deals with the detection of virus in cell culture and covers adequately the observation of cytopathic effect and the haemadsorption technique to elucidate the presence of viral agents which do not produce an observable cellular change. The third section covers identification of viral isolates by determining (1) Nucleic acid type, (2) Chloroform or ether sensitivity, and (3) Sensitivity to acid. The methods described require an exorbitant supply of tissue culture tubes and a good deal of time, both these prerequisites impracticable in the current situation in a diagnostic laboratory. There is no description of the more commonly used methods, the neutralisation of viruses or the technique of haemagglutination-inhibition, but these are given as a reference at the end of the chapter.

The second part, entitled Serologic Methods for the Diagnosis of Viral Infections: The Complement-Fixation Test, gives a clear description of the basis of the complement reaction and brief mention is made to the haemagglutination-inhibition test and its use in serology. The complement-fixation test is then described in great detail for 43 pages. A challenge to the concentration!

If the basic precept of this book is to provide laboratory technologists with a basic understanding of the main techniques of virology, then the subject matter dealt with is too limited to be of adequate value and lacks relevance to currently widely used techniques in diagnostic virology.

Elizabeth Poole.

Symposia of the British Society for Parasitology Volume 15, Parasite Invasion. Edited by Angela E. R. Taylor and R. Muller. Published Blackwell Scientific Publications, Oxford, London, Edinburgh, Melbourne. Price $NZ15.55. Obtainable from N. M. Peryer Ltd., Christchurch.

This 155-page soft-covered volume contains a collection of six papers, presented at the fifteenth autumn symposium of the British Society of Parasitology held in October, 1976.

The papers include: Invasion of the Host Cell by Coccidia; Invasion of Red Cells by Plasmodia; Physiological Changes during the Life-Cycle of Protozoan Parasites; The Entry of Viruses into Cells; The Passage of Helminths through Tissue Barriers; and Energy Metabolism and Infection in Helminths.

As well as discussing the invasion of host cells by several species of parasites, other aspects relating to invasion are also considered. These include problems confronting the parasite in reaching the host cell, as well as physical and chemical changes which may be a necessary prelude to invasion. Other aspects either directly or indirectly related to invasion are considered. For example, the invasion of red cells by plasmodia is preceded by a description of the structure and formation of the merozoite, its release from the schizont, extracellular transit and adhesion to the host cell.

An orphan amongst the eucaryons, the section devoted to viruses gives a lucid account of viral specificity and entry into host cells.

A number of interesting photomicrographs and diagrams accompany the text.

This small volume covers in depth a narrow but important area of parasitology. The book can be recommended to the technologist who wishes to be informed on recent concepts relating to parasite invasion.

A. F. Harper.

Erratum. Fundamental Skills in Serology by Leila J. Walker and Howard Taub. Published by Charles C. Thomas, Springfield, Illinois. Author's name mis-spelt in March issue.

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(1) Klein, G. C. and Jones, W. L. : Applied Microbiol. 21 : 257, 1971.
(2) Janeff, J., Janeff, D., Taranta, A., & Cohen, H. : Lab. Med., 1971 (in press).

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Index to Volume 31

Index to Advertisers

Contents